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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,950	03/07/2002	Sophie Gaubert	02043	2908

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 11/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,950	GAUBERT ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-19,21-33 and 35-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-19,21-33 and 35-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response dated 9-22-06 is acknowledged.

Claims included in the prosecution are 16-19, 21-33 and 35-65.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 16-17, 21-29 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Haan (Vaccines 13, No. 2, pp. 155-162, 1995).

Haan et al teach that intra-nasal administration of multilamellar vesicles containing influenza viral sub-units Results in an induction of both systemic IgG and secretary IgA responses compared with the antigen alone. The response includes both mucosal and systemic responses. The liposomes are made of phosphatidylcholine, cholesterol and DCP (abstract, Materials and Methods and Discussion section). The reference meets the requirements of instant claims.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that the claimed invention is directed to administration of multilamellar vesicles with an onion like structure having an inte4rnal liquid crystal structure formed by stack of concentric bilayers based on amphiphilic agents alternating with layers of water and that as discussed in the interview, De Haan discloses conventional liposomes, whereas the claimed invention is directed to the use of

multilamellar vesicles as disclosed in the Roux et al reference. This argument is not persuasive since the differences argued by applicant are not reflected in the claims. Multilamellar vesicles are onion like structures characterized by concentric membrane bilayers each separated from the next by a layer of water. The examiner cites US 4,522,803 in this context (col. 2, lines 27-34).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 16-17 and 21-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haan et al (Vaccines 13, no. 2, pp. 155-162, 1995) by itself or in combination with Roux (5,908,697) or vice versa.

As discussed extensively in the previous action, Haan et al teach that intra-nasal administration of multilamellar vesicles containing influenza viral sub-units Results in an induction of both systemic IgG and secretary IgA responses compared with the antigen alone (abstract, Materials and Methods and Discussion section).

As also discussed before, Roux discloses active principle carriers containing lecithin (phospholipid) and sucrose ester and the other surfactants. The structures disclosed by Roux are multilamellar vesicles with an onion like structure having an

internal liquid crystal structure formed by a stack of concentric bilayers. According to Roux, these vesicles have certain advantages, which include less sensitivity to bacterial contamination. The vesicles have diameters of 0.1 and 50 microns. The two surfactants according to Roux have HLB values between 3 and 7 and 8-15 respectively (abstract, col. 3, lines 4-27; col. 5, line 40 through col. 7, line 40; Examples and claims). What are lacking in Roux are the teachings of using an antigen as active principle and mucosal administration of the composition to elicit an immune response.

As discussed above, multilamellar liposomes have onion like structure with concentric lipid bilayers separated by aqueous medium. Assuming that Haan's multilamellar liposomes are different from instant liposomes, it is deemed obvious to use multi-lamellar liposomes containing lecithin and sucrose esters of Roux would have been obvious to one of ordinary skill in the art because of the advantages taught by Roux. Alternately, the use of antigen as the active principle and administer the composition of Roux mucosally, with a reasonable expectation of success, since the reference of Haan shows the enhancement of immune response when antigens are administered mucosally in multi-lamellar liposomes compared to antigen alone. Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Roux et al does disclose the vesicles of the invention, but does not disclose or suggest using such vesicles as carriers for antigens. Applicant further argues that since De Haan et al and Roux et al both involve liposomal structures, the question is then whether one could expect to substitute the structures of Roux et al for the conventional liposomes of De Haan et al and expect to achieve the same or

improved results. According to applicant, the results are not the same, because the mechanism of action of De Haan et al is entirely different from that of the invention. These arguments are not persuasive. First of all, since liposomes are known drug and antigen carriers irrespective of whether they are unilamellar or multilamellar in nature. Therefore, one would expect liposomes of Roux liposomes to act in a similar way. Secondly, arguments that the mechanism of action is different without any experimental evidence to show unexpected results are deemed to be speculative in nature. Applicant argues that De Haan states quite clearly that the liposomes used must be negatively charged and on the contrary, the claimed invention does not require negatively charged liposomes. This argument is not persuasive since instant claim language does not exclude negatively charged lipids. Similarly applicant's arguments that De Haan et al utilize large excess of liposomes, a ratio not lower than 500:1 are not persuasive since instant claims do not recite any ratios at all. De Haan's method involves the administration of the antigen by the same method. Instant claims do not differentiate over Haan's teachings. As pointed out before, if the antigen is liberated from the liposomes before reaching the lungs according to applicant, then wont the same alveolar macrophages capture the liberated antigen also? Applicant's arguments that one of ordinary skill in the art would not be motivated to use more stable liposomes as in instant invention (same as those taught by Roux) thus, are not found to be persuasive. It is the examiner's position that one of ordinary skill in the art would be motivated to use Roux's liposomes for the advantages taught by Roux (who teaches the same claimed liposomes).

5. Claims 18-19 and 36-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haan et al (Vaccines 13, no. 2, pp. 155-162, 1995) by itself or in combination with Roux (5,908,697) as set forth above, in further combination with combination with Doerschuk (5,702, 946).

The teachings of Haan et al and Roux have been discussed above. What is lacking in these references is the purification of the immunoglobulins.

The reference of Doerschuk teaches the conventional techniques of purifying the immunoglobulins col. 9, lines 25-30; col. 14, line 50).

The purification of the antibodies produced by the administration of the antigen containing multilamellar vesicles would have been obvious to one of ordinary skill in the art since purification of antibodies by conventional methods is known in the art as evident from Doerschuk.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Doerschuk does not cure the defects of De Haan and Roux references. This argument is not persuasive since this reference is combined for its teachings of the purification of immunoglobulins and the method of purification would be the same irrespective of the carriers used for the administration of the antigens.

6. Claims 16-19, 21-33 and 35-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wassef et al (Immunomethods, 4, pp. 217-222, 1994) in combination with Haan et al (Vaccines 13, no. 2, pp. 155-162, 1995) by itself or in combination with Doerschuk (5,702, 946) and Roux (5,908,697) all cited above.

Wassef et al teach the successful use of multilamellar vesicles as carriers for vaccines (note abstract, pages 218-220). Wassef et al although teach that liposomal vaccines have been administered by many routes, they do not specifically teach mucosal route of administration. Wassef et al's disclosure also lacks specifics about multilamellar vesicles.

The teachings of Haan et al, and those of Doerschuk, and Roux have been discussed above.

The use of Roux's multilamellar vesicles for encapsulating an antigen and delivering the composition mucosally would have been obvious to one of ordinary skill in the art because of the advantages of such liposomes taught by Roux and the enhancement of the immune response when administered mucosally as seen from Haan et al. The purification of the antibodies produced by the administration of the antigen containing multilamellar vesicles would have been obvious to one of ordinary skill in the art since purification of antibodies by conventional methods is known in the art as evident from Doerschuk.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Wassef does not disclose or suggest mucosal administration and that the liposomes used are conventional liposomes. These arguments are not persuasive since the mucosal administration is taught by De Haan and since as pointed out above, instant claims do not distinguish apparent conventional liposomes of Wassef and instant liposomes. Applicant's arguments regarding negatively charged liposomes have already been addressed by the examiner.

The examiner has already suggested a showing of unexpected results obtained by comparison of De Haan's liposomes containing the antigen with instant liposomes containing the same antigen during the interview dated 8-29-05.

7. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/G S Kishore/

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK